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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *
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FILE 'HOME' ENTERED AT 13:49:27 ON 10 JAN 2006

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:49:44 ON 10 JAN 2006

 FILE LAST UPDATED: 7 JAN 2006 (20060107/UP).  FILE COVERS 1950 TO DATE.

 => s uncoupl?
L1       15992 UNCOUPL?

=> s l1(p) receptor#
        725556 RECEPTOR#
L2        2638 L1(P) RECEPTOR#

=> s l2(p)G
        556021 G
L3          780 L2(P)G

=> s l3(p) ident?
       1076690 IDENT?
L4          100 L3(P) IDENT?

=> d 1-100 ti so

L4   ANSWER 1 OF 100     MEDLINE on STN
TI   Hydrogen peroxide causes uncoupling of dopamine D1-like receptors from G
     proteins via a mechanism involving protein kinase C and G-protein-coupled
     receptor kinase 2.
SO   Free radical biology & medicine, (2006 Jan 1) 40 (1) 13-20.  Electronic
     Publication: 2005-09-08.
     Journal code: 8709159. ISSN: 0891-5849.

L4   ANSWER 2 OF 100     MEDLINE on STN
TI   Human adenosine A(3) receptor leads to intracellular Ca(2+) mobilization
     but is insufficient to activate the signaling pathway via phosphoinositide
     3-kinase gamma in mice.
SO   Biochemical pharmacology, (2005 Nov 15) 70 (10) 1487-96.  Electronic
     Publication: 2005-09-12.
     Journal code: 0101032. ISSN: 0006-2952.

L4   ANSWER 3 OF 100     MEDLINE on STN
TI   Osteoblast calcium-sensing receptor has characteristics of ANF/7TM
     receptors.
SO   Journal of cellular biochemistry, (2005 Aug 15) 95 (6) 1081-92.
     Journal code: 8205768. ISSN: 0730-2312.

L4   ANSWER 4 OF 100     MEDLINE on STN
TI   Self-limitation of intravenous tocolysis with beta2-adrenergic agonists is
     mediated through receptor G protein uncoupling.
SO   Journal of clinical endocrinology and metabolism, (2005 May) 90 (5)
     2882-7.  Electronic Publication: 2005-02-22.
     Journal code: 0375362. ISSN: 0021-972X.

L4   ANSWER 5 OF 100     MEDLINE on STN
TI   Estrogen modulation of hypothalamic neurons: activation of multiple
     signaling pathways and gene expression changes.
SO   Steroids, (2005 May-Jun) 70 (5-7) 397-406.  Electronic Publication:
     2005-04-21. Ref: 127
     Journal code: 0404536. ISSN: 0039-128X.

L4   ANSWER 6 OF 100     MEDLINE on STN
TI   The natural mutation encoding a C terminus-truncated 5-hydroxytryptamine
     2B receptor is a gain of proliferative functions.
SO   Molecular pharmacology, (2005 Apr) 67 (4) 983-91.  Electronic Publication:
     2004-12-29.
     Journal code: 0035623. ISSN: 0026-895X.

L4   ANSWER 7 OF 100     MEDLINE on STN
TI   Antiepileptic popular ketogenic diet: emerging twists in an ancient story.
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SO Progress in neurobiology, (2005 Jan) 75 (1) 1-28. Electronic Publication: 2005-01-27. Ref: 220
Journal code: 0370121. ISSN: 0301-0082.

L4 ANSWER 8 OF 100 MEDLINE on STN
TI Interaction between mGluR8 and calcium channels in photoreceptors is sensitive to pertussis toxin and occurs via G protein betagamma subunit signaling.
SO Investigative ophthalmology & visual science, (2005 Jan) 46 (1) 287-91.
Journal code: 7703701. ISSN: 0146-0404.

L4 ANSWER 9 OF 100 MEDLINE on STN
TI Regulation of corticotropin-releasing hormone receptor type 1alpha signaling: structural determinants for G protein-coupled receptor kinase-mediated phosphorylation and agonist-mediated desensitization.
SO Molecular endocrinology (Baltimore, Md.), (2005 Feb) 19 (2) 474-90.
Electronic Publication: 2004-10-21.
Journal code: 8801431. ISSN: 0888-8809.

L4 ANSWER 10 OF 100 MEDLINE on STN
TI Peptide ligand binding properties of the corticotropin-releasing factor (CRF) type 2 receptor: pharmacology of endogenously expressed receptors, G-protein-coupling sensitivity and determinants of CRF2 receptor selectivity.
SO Peptides, (2005 Mar) 26 (3) 457-70.
Journal code: 8008690. ISSN: 0196-9781.

L4 ANSWER 11 OF 100 MEDLINE on STN
TI Distinct molecular mechanisms for agonist peptide binding to types A and B cholecystokinin receptors demonstrated using fluorescence spectroscopy.
SO Journal of biological chemistry, (2005 Jan 14) 280 (2) 1044-50.
Electronic Publication: 2004-11-01.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 12 OF 100 MEDLINE on STN
TI Arrestins and G-protein--coupled receptors: an on-again, off-again relationship.
SO Drug news & perspectives, (1998 Mar) 11 (2) 73-81.
Journal code: 8809164. ISSN: 0214-0934.

L4 ANSWER 13 OF 100 MEDLINE on STN
TI Mu-opioid receptor desensitization: is morphine different?.
SO British journal of pharmacology, (2004 Nov) 143 (6) 685-96. Electronic Publication: 2004-10-25. Ref: 70
Journal code: 7502536. ISSN: 0007-1188.

L4 ANSWER 14 OF 100 MEDLINE on STN
TI Assays for G-protein-coupled receptor signaling using RGS-insensitive Galpha subunits.
SO Methods in enzymology, (2004) 389 155-69. Ref: 22
Journal code: 0212271. ISSN: 0076-6879.

L4 ANSWER 15 OF 100 MEDLINE on STN
TI The pasteurella multocida toxin interacts with signalling pathways to perturb cell growth and differentiation.
SO International journal of medical microbiology : IJMM, (2004 Apr) 293 (7-8) 505-12. Ref: 49
Journal code: 100898849. ISSN: 1438-4221.

L4 ANSWER 16 OF 100 MEDLINE on STN
TI Heterotrimeric G protein subunits are located on rat liver endosomes.
SO BMC physiology [electronic resource], (2004 Jan 7) 4 1. Electronic Publication: 2004-01-07.
Journal code: 101088687. ISSN: 1472-6793.

L4 ANSWER 17 OF 100 MEDLINE on STN
TI Conformational states of the corticotropin releasing factor 1 (CRF1) receptor: detection, and pharmacological evaluation by peptide ligands.
SO Peptides, (2003 Dec) 24 (12) 1881-97.
Journal code: 8008690. ISSN: 0196-9781.

L4 ANSWER 18 OF 100 MEDLINE on STN
TI Estrogen modulation of G-protein-coupled receptor activation of potassium channels in the central nervous system.
SO Annals of the New York Academy of Sciences, (2003 Dec) 1007 6-16. Ref: 78
Journal code: 7506858. ISSN: 0077-8923.

L4 ANSWER 19 OF 100 MEDLINE on STN
TI Heterotrimeric G protein Gi is involved in a signal transduction pathway for ATP release from erythrocytes.
SO American journal of physiology. Heart and circulatory physiology, (2004 Mar) 286 (3) H940-5. Electronic Publication: 2003-11-13.
Journal code: 100901228. ISSN: 0363-6135.

L4 ANSWER 20 OF 100 MEDLINE on STN
TI Dual inhibition of beta-adrenergic and angiotensin II receptors by a single antagonist: a functional role for receptor-receptor interaction in vivo.
SO Circulation, (2003 Sep 30) 108 (13) 1611-8. Electronic Publication: 2003-09-08.
Journal code: 0147763. ISSN: 1524-4539.

L4 ANSWER 21 OF 100 MEDLINE on STN
TI Identification of two serine residues essential for agonist-induced 5-HT2A receptor desensitization.
SO Biochemistry, (2003 Sep 16) 42 (36) 10853-62.
Journal code: 0370623. ISSN: 0006-2960.

L4 ANSWER 22 OF 100 MEDLINE on STN
TI Mutational uncoupling of alpha1A-adrenergic receptors from G proteins also uncouples mitogenic and transcriptional responses in PC12 cells.
SO Journal of pharmacology and experimental therapeutics, (2003 Aug) 306 (2) 471-7. Electronic Publication: 2003-04-30.
Journal code: 0376362. ISSN: 0022-3565.

L4 ANSWER 23 OF 100 MEDLINE on STN
TI C5L2, a nonsignaling C5A binding protein.
SO Biochemistry, (2003 Aug 12) 42 (31) 9406-15.
Journal code: 0370623. ISSN: 0006-2960.

L4 ANSWER 24 OF 100 MEDLINE on STN
TI Endogenous G protein-coupled receptor kinase 6 triggers homologous beta-adrenergic receptor desensitization in primary uterine smooth muscle cells.
SO Endocrinology, (2003 Jul) 144 (7) 3058-66.
Journal code: 0375040. ISSN: 0013-7227.

L4 ANSWER 25 OF 100 MEDLINE on STN
TI G protein-coupled receptor Kinase 2/G alpha q/11 interaction. A novel surface on a regulator of G protein signaling homology domain for binding G alpha subunits.
SO Journal of biological chemistry, (2003 Feb 21) 278 (8) 6050-8. Electronic Publication: 2002-11-08.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 26 OF 100 MEDLINE on STN
TI Constitutive activity of G-protein-coupled receptors: cause of disease and common property of wild-type receptors.
SO Naunyn-Schmiedeberg's archives of pharmacology, (2002 Nov) 366 (5) 381-416. Electronic Publication: 2002-09-06. Ref: 240
Journal code: 0326264. ISSN: 0028-1298.

L4 ANSWER 27 OF 100 MEDLINE on STN
TI Apparent loss-of-function mutant GPCRs revealed as constitutively desensitized receptors.
SO Biochemistry, (2002 Oct 8) 41 (40) 11981-9.
Journal code: 0370623. ISSN: 0006-2960.

L4 ANSWER 28 OF 100 MEDLINE on STN
TI Conserved helix 7 tyrosine acts as a multistate conformational switch in the 5HT2C receptor. Identification of a novel "locked-on" phenotype and double revertant mutations.
SO Journal of biological chemistry, (2002 Sep 27) 277 (39) 36577-84. Electronic Publication: 2002-07-26.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 29 OF 100 MEDLINE on STN
TI Characterization of cholera toxin B subunit-induced Ca(2+) influx in neuroblastoma cells: evidence for a voltage-independent GM1 ganglioside-associated Ca(2+) channel.
SO Journal of neuroscience research, (2002 Sep 1) 69 (5) 669-80.
Journal code: 7600111. ISSN: 0360-4012.

L4 ANSWER 30 OF 100 MEDLINE on STN
TI Identification of a signal transduction switch in the chemokine receptor CXCR1.
SO Journal of biological chemistry, (2002 Aug 30) 277 (35) 31563-6. Electronic Publication: 2002-06-20.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 31 OF 100 MEDLINE on STN
TI Peripheral mechanisms involved with catabolism.
SO Current opinion in clinical nutrition and metabolic care, (2002 Jul) 5 (4) 419-26. Ref: 49
Journal code: 9804399. ISSN: 1363-1950.

L4 ANSWER 32 OF 100 MEDLINE on STN
TI Aripiprazole, a novel antipsychotic, is a high-affinity partial agonist at human dopamine D2 receptors.
SO Journal of pharmacology and experimental therapeutics, (2002 Jul) 302 (1) 381-9.
Journal code: 0376362. ISSN: 0022-3565.

L4 ANSWER 33 OF 100 MEDLINE on STN
TI Effect of pertussis toxin and N-ethylmaleimide on voltage-dependent and -independent calcium current modulation in serotonergic neurons.
SO Neuroscience, (2002) 111 (1) 207-14.
Journal code: 7605074. ISSN: 0306-4522.

L4 ANSWER 34 OF 100 MEDLINE on STN
TI Discrimination of galanin receptor subtypes in RINm5F cells by structurally different galanin radioligands.
SO Peptides, (2002 Mar) 23 (3) 545-53.
Journal code: 8008690. ISSN: 0196-9781.

L4 ANSWER 35 OF 100 MEDLINE on STN
TI Biased inhibition by a suramin analogue of A1-adenosine receptor/G protein coupling in fused receptor/G protein tandems: the A1-adenosine receptor is predominantly coupled to Goalpha in human brain.
SO Naunyn-Schmiedeberg's archives of pharmacology, (2002 Jan) 365 (1) 8-16.
Electronic Publication: 2001-11-07.
Journal code: 0326264. ISSN: 0028-1298.

L4 ANSWER 36 OF 100 MEDLINE on STN
TI Peptides as receptor ligand drugs and their relationship to G-coupled signal transduction.
SO Expert opinion on investigational drugs, (2001 Jun) 10 (6) 1063-73. Ref: 149
Journal code: 9434197. ISSN: 1354-3784.

L4 ANSWER 37 OF 100 MEDLINE on STN
TI Magnetic fields (MF) of 50 Hz at 1.2 microT as well as 100 microT cause uncoupling of inhibitory pathways of adenylyl cyclase mediated by melatonin 1a receptor in MF-sensitive MCF-7 cells.
SO Carcinogenesis, (2001 Jul) 22 (7) 1043-8.
Journal code: 8008055. ISSN: 0143-3334.

L4 ANSWER 38 OF 100 MEDLINE on STN
TI Molecular scaffold protein and cellular responses.
SO Trends in endocrinology and metabolism: TEM, (2001 Jul) 12 (5) 184-6.
Journal code: 9001516. ISSN: 1043-2760.

L4 ANSWER 39 OF 100 MEDLINE on STN
TI Concomitant increase of G protein-coupled receptor kinase activity and uncoupling of beta-adrenergic receptors in rat myometrium at parturition.
SO Endocrinology, (2001 May) 142 (5) 1899-905.
Journal code: 0375040. ISSN: 0013-7227.

L4 ANSWER 40 OF 100 MEDLINE on STN
TI The cardiac beta-adrenoceptor-G-protein(s)-adenylyl cyclase system in monocrotaline-treated rats.
SO Journal of molecular and cellular cardiology, (2000 Dec) 32 (12) 2315-26.
Journal code: 0262322. ISSN: 0022-2828.

L4 ANSWER 41 OF 100 MEDLINE on STN
TI Selective resistance to parathyroid hormone caused by a novel uncoupling mutation in the carboxyl terminus of G alpha(s). A cause of pseudohypoparathyroidism type Ib.
SO Journal of biological chemistry, (2001 Jan 5) 276 (1) 165-71.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 42 OF 100 MEDLINE on STN
TI Studies of the synergistic effect of the Trp/Arg64 polymorphism of the beta3-adrenergic receptor gene and the -3826 A-->G variant of the uncoupling protein-1 gene on features of obesity and insulin resistance in a population-based sample of 379 young Danish subjects.
SO Journal of clinical endocrinology and metabolism, (2000 Sep) 85 (9) 3151-4.
Journal code: 0375362. ISSN: 0021-972X.

L4 ANSWER 43 OF 100 MEDLINE on STN
TI The heat shock cognate protein hsc73 assembles with A(1) adenosine receptors to form functional modules in the cell membrane.
SO Molecular and cellular biology, (2000 Jul) 20 (14) 5164-74.
Journal code: 8109087. ISSN: 0270-7306.

L4 ANSWER 44 OF 100 MEDLINE on STN
TI Thermodynamically distinct high and low affinity states of the A(1) adenosine receptor induced by G protein coupling and guanine nucleotide

ligation states of G proteins.
SO British journal of pharmacology, (2000 Jun) 130 (3) 595-604.
Journal code: 7502536. ISSN: 0007-1188.

L4 ANSWER 45 OF 100 MEDLINE on STN
TI High-affinity binding of urocortin and astressin but not CRF to G protein-uncoupled CRFR1.
SO Peptides, (1999 Nov) 20 (11) 1311-9.
Journal code: 8008690. ISSN: 0196-9781.

L4 ANSWER 46 OF 100 MEDLINE on STN
TI Feedback inhibition of G protein-coupled receptor kinase 2 (GRK2) activity by extracellular signal-regulated kinases.
SO Journal of biological chemistry, (1999 Dec 3) 274 (49) 34531-4.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 47 OF 100 MEDLINE on STN
TI Agonist induced conformation alteration of neurotensin receptor and the mechanism behind Na+ inhibition of 125I-NT binding.
SO Journal of receptor and signal transduction research, (1999 Nov) 19 (6) 995-1021.
Journal code: 9509432. ISSN: 1079-9893.

L4 ANSWER 48 OF 100 MEDLINE on STN
TI Nurr1, an orphan nuclear receptor, is a transcriptional activator of endogenous tyrosine hydroxylase in neural progenitor cells derived from the adult brain.
SO Development (Cambridge, England), (1999 Sep) 126 (18) 4017-26.
Journal code: 8701744. ISSN: 0950-1991.

L4 ANSWER 49 OF 100 MEDLINE on STN
TI G-protein coupled receptor kinases as modulators of G-protein signalling.
SO Journal of physiology, (1999 May 15) 517 (Pt 1) 5-23. Ref: 186
Journal code: 0266262. ISSN: 0022-3751.

L4 ANSWER 50 OF 100 MEDLINE on STN
TI Lesion of septal-hippocampal neurons with 192 IgG-saporin alters function of M1 muscarinic receptors.
SO Neuropharmacology, (1999 Apr) 38 (4) 579-86.
Journal code: 0236217. ISSN: 0028-3908.

L4 ANSWER 51 OF 100 MEDLINE on STN
TI Cellular trafficking of G protein-coupled receptor/beta-arrestin endocytic complexes.
SO Journal of biological chemistry, (1999 Apr 16) 274 (16) 10999-1006.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 52 OF 100 MEDLINE on STN
TI Identification of protein kinase C phosphorylation sites involved in phorbol ester-induced desensitization of the histamine H1 receptor.
SO Molecular pharmacology, (1999 Apr) 55 (4) 735-42.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 53 OF 100 MEDLINE on STN
TI Altered Gq/G11 guanine nucleotide regulatory protein expression in a rat model of hepatocellular carcinoma: role in mitogenesis.
SO Hepatology (Baltimore, Md.), (1999 Feb) 29 (2) 371-8.
Journal code: 8302946. ISSN: 0270-9139.

L4 ANSWER 54 OF 100 MEDLINE on STN
TI The cytoplasmic tails of protease-activated receptor-1 and substance P receptor specify sorting to lysosomes versus recycling.
SO Journal of biological chemistry, (1999 Jan 22) 274 (4) 2216-24.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 55 OF 100 MEDLINE on STN
TI Reciprocal in vivo regulation of myocardial G protein-coupled receptor kinase expression by beta-adrenergic receptor stimulation and blockade.
SO Circulation, (1998 Oct 27) 98 (17) 1783-9.
Journal code: 0147763. ISSN: 0009-7322.

L4 ANSWER 56 OF 100 MEDLINE on STN
TI Second site suppressor mutations of a GTPase-deficient G-protein alpha-subunit. Selective inhibition of Gbeta gamma-mediated signaling.
SO Journal of biological chemistry, (1998 Oct 30) 273 (44) 28597-602.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 57 OF 100 MEDLINE on STN
TI Mutation of a putative amphipathic alpha-helix in the third intracellular domain of the platelet-activating factor receptor disrupts receptor/G protein coupling and signaling.
SO Molecular pharmacology, (1998 Mar) 53 (3) 451-8.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 58 OF 100 MEDLINE on STN
TI Selective uncoupling of RGS action by a single point mutation in the G protein alpha-subunit.
SO Journal of biological chemistry, (1998 Mar 6) 273 (10) 5780-4.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 59 OF 100 MEDLINE on STN
TI Gsalpha-selective G protein antagonists.
SO Proceedings of the National Academy of Sciences of the United States of America, (1998 Jan 6) 95 (1) 346-51.
Journal code: 7505876. ISSN: 0027-8424.

L4 ANSWER 60 OF 100 MEDLINE on STN
TI The alpha1B-adrenergic receptor subtype activates the phospholipase C signaling pathway in rat myometrium at parturition.
SO Biology of reproduction, (1997 Nov) 57 (5) 1175-82.
Journal code: 0207224. ISSN: 0006-3363.

L4 ANSWER 61 OF 100 MEDLINE on STN
TI Induction of multiple effects on adenylyl cyclase regulation by chronic activation of the human A3 adenosine receptor.
SO Molecular pharmacology, (1997 Oct) 52 (4) 632-40.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 62 OF 100 MEDLINE on STN
TI Internalization of the m2 muscarinic acetylcholine receptor. Arrestin-independent and -dependent pathways.
SO Journal of biological chemistry, (1997 Sep 19) 272 (38) 23682-9.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 63 OF 100 MEDLINE on STN
TI Somatostatin inhibits interleukin 6 release from rat cortical type I astrocytes via the inhibition of adenylyl cyclase.
SO Biochemical and biophysical research communications, (1997 Jun 9) 235 (1) 242-8.
Journal code: 0372516. ISSN: 0006-291X.

L4 ANSWER 64 OF 100 MEDLINE on STN
TI Order of application determines the interaction between phorbol esters and GTP-gamma-S in dorsal raphe neurons: evidence that the effect of 5-HT is modified upstream of the G protein Ca channel interaction.
SO Journal of neurophysiology, (1997 May) 77 (5) 2697-703.
Journal code: 0375404. ISSN: 0022-3077.

L4 ANSWER 65 OF 100 MEDLINE on STN
TI Oxytocin receptor-mediated activation of phosphoinositidase C and elevation of cytosolic calcium in the gonadotrope-derived alphaT3-1 cell line.
SO Endocrinology, (1997 May) 138 (5) 2049-55.
Journal code: 0375040. ISSN: 0013-7227.

L4 ANSWER 66 OF 100 MEDLINE on STN
TI Mechanisms of beta-adrenergic receptor desensitization: from molecular biology to heart failure.
SO Basic research in cardiology, (1996) 91 Suppl 2 29-34. Ref: 62
Journal code: 0360342. ISSN: 0300-8428.

L4 ANSWER 67 OF 100 MEDLINE on STN
TI Purification and reconstitution of a recombinant human neurokinin-1 receptor.
SO Journal of receptor and signal transduction research, (1996 May-Jul) 16 (3-4) 191-207.
Journal code: 9509432. ISSN: 1079-9893.

L4 ANSWER 68 OF 100 MEDLINE on STN
TI Inhibition of receptor/G protein coupling by suramin analogues.
SO Molecular pharmacology, (1996 Aug) 50 (2) 415-23.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 69 OF 100 MEDLINE on STN
TI Analysis of granulocyte colony stimulating factor receptor isoforms, polymorphisms and mutations in normal haemopoietic cells and acute myeloid leukaemia blasts.
SO British journal of haematology, (1996 Jun) 93 (3) 527-33.
Journal code: 0372544. ISSN: 0007-1048.

L4 ANSWER 70 OF 100 MEDLINE on STN
TI Lack of discrimination by agonists for D2 and D3 dopamine receptors.
SO Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology, (1995 Jul) 12 (4) 335-45.
Journal code: 8904907. ISSN: 0893-133X.

L4 ANSWER 71 OF 100 MEDLINE on STN
TI Truncation of the C-terminal tail of the follitropin receptor does not impair the agonist- or phorbol ester-induced receptor phosphorylation and uncoupling.
SO Journal of biological chemistry, (1995 Nov 3) 270 (44) 26683-9.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 72 OF 100 MEDLINE on STN
TI Reciprocal binding properties of 5-hydroxytryptamine type 2C receptor agonists and inverse agonists.
SO Molecular pharmacology, (1994 Nov) 46 (5) 937-42.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 73 OF 100 MEDLINE on STN
TI Antagonists of bradykinin that stabilize a G-protein-uncoupled state of the B2 receptor act as inverse agonists in rat myometrial cells.
SO Journal of biological chemistry, (1994 Oct 21) 269 (42) 25970-3.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 74 OF 100 MEDLINE on STN
TI The conserved NPXnY motif present in the gastrin-releasing peptide receptor is not a general sequestration sequence.
SO Journal of biological chemistry, (1994 Aug 26) 269 (34) 21755-61.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 75 OF 100 MEDLINE on STN
TI Chimeric G alpha s/G alpha i2 proteins define domains on G alpha s that interact with tubulin for beta-adrenergic activation of adenylyl cyclase.
SO Journal of biological chemistry, (1994 Aug 26) 269 (34) 21748-54.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 76 OF 100 MEDLINE on STN
TI Properties of G-protein modulated receptor-adenylyl cyclase system in myocardium of spontaneously hypertensive rats treated with adriamycin.
SO International journal of cardiology, (1994 Mar 15) 44 (1) 9-18.
Journal code: 8200291. ISSN: 0167-5273.

L4 ANSWER 77 OF 100 MEDLINE on STN
TI Identification of a human delta opioid receptor: cloning and expression.
SO Life sciences, (1994) 54 (25) PL463-9.
Journal code: 0375521. ISSN: 0024-3205.

L4 ANSWER 78 OF 100 MEDLINE on STN
TI Second messenger signalling in olfaction.
SO Ciba Foundation symposium, (1993) 179 97-109; discussion 109-14, 147-9.
Ref: 27
Journal code: 0356636. ISSN: 0300-5208.

L4 ANSWER 79 OF 100 MEDLINE on STN
TI Continuous spectrofluorometric analysis of formyl peptide receptor ternary complex interactions.
SO Molecular pharmacology, (1994 Jan) 45 (1) 65-73.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 80 OF 100 MEDLINE on STN
TI Guanine nucleotide binding proteins mediate D2 dopamine receptor activation of a potassium channel in rat lactotrophs.
SO Journal of physiology, (1993 Mar) 462 563-78.
Journal code: 0266262. ISSN: 0022-3751.

L4 ANSWER 81 OF 100 MEDLINE on STN
TI Photoaffinity labelling and radiation inactivation of the leukotriene B4 receptor in human myeloid cells.
SO European journal of pharmacology, (1993 Jan 15) 244 (2) 161-73.
Journal code: 1254354. ISSN: 0014-2999.

L4 ANSWER 82 OF 100 MEDLINE on STN
TI Regulation of spontaneous opening of muscarinic K+ channels in rabbit atrium.
SO Journal of physiology, (1991 Feb) 433 589-613.
Journal code: 0266262. ISSN: 0022-3751.

L4 ANSWER 83 OF 100 MEDLINE on STN
TI Catabolism of hemoglobin-haptoglobin complex in microsome subfractions.
SO Chemical & pharmaceutical bulletin, (1992 Jul) 40 (7) 1847-51.
Journal code: 0377775. ISSN: 0009-2363.

L4 ANSWER 84 OF 100 MEDLINE on STN
TI Occupancy of G alpha s-linked receptors uncouples chemoattractant receptors from their stimulus-transduction mechanisms in the neutrophil.
SO Blood, (1992 Aug 15) 80 (4) 1052-7.
Journal code: 7603509. ISSN: 0006-4971.

L4 ANSWER 85 OF 100 MEDLINE on STN
TI Ligand-mediated internalization of glucagon receptors in intact rat liver.
SO Endocrinology, (1992 Jul) 131 (1) 447-57.
Journal code: 0375040. ISSN: 0013-7227.

L4 ANSWER 86 OF 100 MEDLINE on STN
TI GAP domains responsible for ras p21-dependent inhibition of muscarinic atrial K+ channel currents.
SO Science, (1992 Jan 10) 255 (5041) 192-4.
Journal code: 0404511. ISSN: 0036-8075.

L4 ANSWER 87 OF 100 MEDLINE on STN
TI Brain somatostatin receptor-G protein interaction. G alpha C-terminal antibodies demonstrate coupling of the soluble receptor with Gi(1-3) but not with Go.
SO Journal of biological chemistry, (1992 Feb 15) 267 (5) 2960-5.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 88 OF 100 MEDLINE on STN
TI Characterization of solubilized opioid receptors: reconstitution and uncoupling of guanine nucleotide-sensitive agonist binding.
SO Journal of neurochemistry, (1992 Feb) 58 (2) 628-35.
Journal code: 2985190R. ISSN: 0022-3042.

L4 ANSWER 89 OF 100 MEDLINE on STN
TI Identification of the subunits of GTP-binding proteins coupled to somatostatin receptors.
SO Journal of biological chemistry, (1991 Sep 25) 266 (27) 17885-97.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 90 OF 100 MEDLINE on STN
TI Inhibitory GTP-binding regulatory protein Gi3 can couple angiotensin II receptors to inhibition of adenylyl cyclase in hepatocytes.
SO Molecular pharmacology, (1991 Aug) 40 (2) 156-67.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 91 OF 100 MEDLINE on STN
TI Regulation of transmembrane signal transduction of insulin-like growth factor II by competence type growth factors or viral ras p21.
SO Journal of biological chemistry, (1991 Jan 15) 266 (2) 1085-91.
Journal code: 2985121R. ISSN: 0021-9258.

L4 ANSWER 92 OF 100 MEDLINE on STN
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SO American review of respiratory disease, (1990 Dec) 142 (6 Pt 2) S11-5.
Ref: 51
Journal code: 0370523. ISSN: 0003-0805.

L4 ANSWER 93 OF 100 MEDLINE on STN
TI Activation of superoxide formation and lysozyme release in human neutrophils by the synthetic lipopeptide Pam3Cys-Ser-(Lys)4. Involvement of guanine-nucleotide-binding proteins and synergism with chemotactic peptides.
SO Biochemical journal, (1990 May 1) 267 (3) 795-802.
Journal code: 2984726R. ISSN: 0264-6021.

L4 ANSWER 94 OF 100 MEDLINE on STN
TI Effects of a choline-deficient ethionine-supplemented diet on phospholipase C activity in mouse pancreatic acinar cell membranes and in electropermeabilized mouse pancreatic acini.
SO Journal of pharmacology and experimental therapeutics, (1990 May) 253 (2) 847-50.
Journal code: 0376362. ISSN: 0022-3565.

L4 ANSWER 95 OF 100 MEDLINE on STN
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SO Molecular pharmacology, (1990 Feb) 37 (2) 304-10.
Journal code: 0035623. ISSN: 0026-895X.

L4 ANSWER 96 OF 100 MEDLINE on STN
TI Desensitization of alpha 2-adrenergic receptors in NG 108 15 cells by (-)-adrenaline and phorbol 12-myristate 13-acetate.
SO Biochemical journal, (1989 Aug 15) 262 (1) 245-51.
Journal code: 2984726R. ISSN: 0264-6021.

L4 ANSWER 97 OF 100 MEDLINE on STN
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SO Proceedings of the National Academy of Sciences of the United States of America, (1989 May) 86 (10) 3882-6.
Journal code: 7505876. ISSN: 0027-8424.

L4 ANSWER 98 OF 100 MEDLINE on STN
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SO Journal of medicinal chemistry, (1989 Apr) 32 (4) 869-74.
Journal code: 9716531. ISSN: 0022-2623.

L4 ANSWER 99 OF 100 MEDLINE on STN
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SO Klinische Wochenschrift, (1988 Jul 1) 66 (13) 557-64. Ref: 73
Journal code: 2985205R. ISSN: 0023-2173.

L4 ANSWER 100 OF 100 MEDLINE on STN
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SO Acta pathologica, microbiologica, et immunologica Scandinavica. Section A, Pathology, (1986 Jul) 94 (4) 245-52.
Journal code: 8206622. ISSN: 0108-0164.

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(FILE 'HOME' ENTERED AT 13:49:27 ON 10 JAN 2006)

FILE 'MEDLINE' ENTERED AT 13:49:44 ON 10 JAN 2006
L1 15992 S UNCOUPL?
L2 2638 S L1(P) RECEPTOR#
L3 780 S L2(P)G
L4 100 S L3(P) IDENT?

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L5 1 PERTIS?

=> s pertus?
L6 20722 PERTUS?

=> s l6(p)l1
L7 216 L6(P)L1

=> s l6(p)l2
L8 193 L6(P)L2

=> s l6(p)l3
L9 143 L6(P)L3

=> d 1-143 ti so

L9 ANSWER 1 OF 143 MEDLINE on STN
TI Regulation of limbic status epilepticus by hippocampal galanin type 1 and type 2 receptors.
SO Neuropeptides, (2005 Jun) 39 (3) 277-80. Electronic Publication: 2005-01-28. Ref: 9
Journal code: 8103156. ISSN: 0143-4179.

L9 ANSWER 2 OF 143 MEDLINE on STN
TI Interaction between mGluR8 and calcium channels in photoreceptors is sensitive to pertussis toxin and occurs via G protein betagamma subunit signaling.
SO Investigative ophthalmology & visual science, (2005 Jan) 46 (1) 287-91.
Journal code: 7703701. ISSN: 0146-0404.

L9 ANSWER 3 OF 143 MEDLINE on STN
TI Endogenous regulator of g protein signaling proteins reduce {mu}-opioid receptor desensitization and down-regulation and adenylyl cyclase tolerance in C6 cells.
SO Journal of pharmacology and experimental therapeutics, (2005 Feb) 312 (2) 809-15. Electronic Publication: 2004-09-21.
Journal code: 0376362. ISSN: 0022-3565.

L9 ANSWER 4 OF 143 MEDLINE on STN
TI Assays for G-protein-coupled receptor signaling using RGS-insensitive Galpha subunits.
SO Methods in enzymology, (2004) 389 155-69. Ref: 22
Journal code: 0212271. ISSN: 0076-6879.

L9 ANSWER 5 OF 143 MEDLINE on STN
TI Regulation of dopamine D-receptor activation in vivo by protein phosphatase 2B (calcineurin).
SO Journal of neurochemistry, (2004 Aug) 90 (4) 865-73.

Journal code: 2985190R. ISSN: 0022-3042.

L9 ANSWER 6 OF 143 MEDLINE on STN
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SO BMC cell biology [electronic resource], (2004 May 24) 5 21. Electronic Publication: 2004-05-24.
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L9 ANSWER 7 OF 143 MEDLINE on STN
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SO Journal of pharmacology and experimental therapeutics, (2004 Jul) 310 (1) 215-22. Electronic Publication: 2004-03-10.
Journal code: 0376362. ISSN: 0022-3565.

L9 ANSWER 8 OF 143 MEDLINE on STN
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SO Diabetes, (2004 Apr) 53 (4) 998-1006.
Journal code: 0372763. ISSN: 0012-1797.

L9 ANSWER 9 OF 143 MEDLINE on STN
TI Heterotrimeric G protein Gi is involved in a signal transduction pathway for ATP release from erythrocytes.
SO American journal of physiology. Heart and circulatory physiology, (2004 Mar) 286 (3) H940-5. Electronic Publication: 2003-11-13.
Journal code: 100901228. ISSN: 0363-6135.

L9 ANSWER 10 OF 143 MEDLINE on STN
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SO Molecular therapy : journal of the American Society of Gene Therapy, (2004 Jan) 9 (1) 24-9.
Journal code: 100890581. ISSN: 1525-0016.

L9 ANSWER 11 OF 143 MEDLINE on STN
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SO Biochemical and biophysical research communications, (2003 Jul 11) 306 (4) 959-65.
Journal code: 0372516. ISSN: 0006-291X.

L9 ANSWER 12 OF 143 MEDLINE on STN
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SO Molecular pharmacology, (2003 Mar) 63 (3) 478-88.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 13 OF 143 MEDLINE on STN
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SO Sheng wu hua xue yu sheng wu wu li xue bao Acta biochimica et biophysica Sinica, (2003 Jan) 35 (1) 41-8.
Journal code: 20730160R. ISSN: 0582-9879.

L9 ANSWER 14 OF 143 MEDLINE on STN
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SO Journal of physiology, (2002 Dec 1) 545 (Pt 2) 355-73.
Journal code: 0266262. ISSN: 0022-3751.

L9 ANSWER 15 OF 143 MEDLINE on STN
TI Constitutive activity of G-protein-coupled receptors: cause of disease and common property of wild-type receptors.
SO Naunyn-Schmiedeberg's archives of pharmacology, (2002 Nov) 366 (5) 381-416. Electronic Publication: 2002-09-06. Ref: 240
Journal code: 0326264. ISSN: 0028-1298.

L9 ANSWER 16 OF 143 MEDLINE on STN
TI Involvement of both G(q/11) and G(s) proteins in gonadotropin-releasing hormone receptor-mediated signaling in L beta T2 cells.
SO Journal of biological chemistry, (2002 Aug 30) 277 (35) 32099-108. Electronic Publication: 2002-06-05.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 17 OF 143 MEDLINE on STN
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trafficking.
SO Molecular pharmacology, (2002 Sep) 62 (3) 578-89.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 18 OF 143 MEDLINE on STN
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SO Molecular endocrinology (Baltimore, Md.), (2002 Aug) 16 (8) 1903-11.
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L9 ANSWER 19 OF 143 MEDLINE on STN
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SO Molecular pharmacology, (2002 Jun) 61 (6) 1329-39.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 20 OF 143 MEDLINE on STN
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SO Neuroscience, (2002) 111 (1) 207-14.
Journal code: 7605074. ISSN: 0306-4522.

L9 ANSWER 21 OF 143 MEDLINE on STN
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SO Biochemistry, (2001 Dec 11) 40 (49) 15031-7.
Journal code: 0370623. ISSN: 0006-2960.

L9 ANSWER 22 OF 143 MEDLINE on STN
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SO Experimental cell research, (2001 Nov 15) 271 (1) 189-99.
Journal code: 0373226. ISSN: 0014-4827.

L9 ANSWER 23 OF 143 MEDLINE on STN
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SO Biologicals : journal of the International Association of Biological Standardization, (2001 Jun) 29 (2) 81-95.
Journal code: 9004494. ISSN: 1045-1056.

L9 ANSWER 24 OF 143 MEDLINE on STN
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SO British journal of pharmacology, (2001 Sep) 134 (1) 6-9.
Journal code: 7502536. ISSN: 0007-1188.

L9 ANSWER 25 OF 143 MEDLINE on STN
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SO The Journal of biological chemistry, (2001 Jul 27) 276 (30) 28578-85.
Electronic Publication: 2001-05-18.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 26 OF 143 MEDLINE on STN
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SO Peptides, (2001 Mar) 22 (3) 379-86.
Journal code: 8008690. ISSN: 0196-9781.

L9 ANSWER 27 OF 143 MEDLINE on STN
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SO Journal of neurobiology, (2001 Aug) 48 (2) 87-100.
Journal code: 0213640. ISSN: 0022-3034.

L9 ANSWER 28 OF 143 MEDLINE on STN
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SO Journal of biological chemistry, (2001 Jun 29) 276 (26) 23645-52.
Electronic Publication: 2001-04-20.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 29 OF 143 MEDLINE on STN
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SO Pathologie-biologie, (2001 May) 49 (4) 339-48. Ref: 75
Journal code: 0265365. ISSN: 0369-8114.

L9 ANSWER 30 OF 143 MEDLINE on STN
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SO Neuroendocrinology, (2001 May) 73 (5) 334-43.
Journal code: 0035665. ISSN: 0028-3835.

L9 ANSWER 31 OF 143 MEDLINE on STN
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SO Journal of neurophysiology, (2001 Apr) 85 (4) 1453-60.
Journal code: 0375404. ISSN: 0022-3077.

L9 ANSWER 32 OF 143 MEDLINE on STN
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SO Journal of pharmacology and experimental therapeutics, (2001 Jun) 297 (3) 1152-9.
Journal code: 0376362. ISSN: 0022-3565.

L9 ANSWER 33 OF 143 MEDLINE on STN
TI Ionotropic histamine receptors and H2 receptors modulate supraoptic oxytocin neuronal excitability and dye coupling.
SO Journal of neuroscience : official journal of the Society for Neuroscience, (2001 May 1) 21 (9) 2974-82.
Journal code: 8102140. ISSN: 1529-2401.

L9 ANSWER 34 OF 143 MEDLINE on STN
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SO Neuropharmacology, (2001 Apr) 40 (5) 645-56.
Journal code: 0236217. ISSN: 0028-3908.

L9 ANSWER 35 OF 143 MEDLINE on STN
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SO European journal of pharmacology, (2000 Dec 8) 409 (2) 143-54.
Journal code: 1254354. ISSN: 0014-2999.

L9 ANSWER 36 OF 143 MEDLINE on STN
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SO Proceedings of the National Academy of Sciences of the United States of America, (2000 Nov 7) 97 (23) 12810-5.
Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 37 OF 143 MEDLINE on STN
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SO Comparative biochemistry and physiology. Part B, Biochemistry & molecular biology, (2000 Jan) 125 (1) 103-14.
Journal code: 9516061. ISSN: 1096-4959.

L9 ANSWER 38 OF 143 MEDLINE on STN
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SO Journal of pharmacology and experimental therapeutics, (2000 Aug) 294 (2) 770-7.
Journal code: 0376362. ISSN: 0022-3565.

L9 ANSWER 39 OF 143 MEDLINE on STN
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SO Journal of neuroscience research, (2000 Jul 1) 61 (1) 75-81.
Journal code: 7600111. ISSN: 0360-4012.

L9 ANSWER 40 OF 143 MEDLINE on STN
TI Acetylcholine stimulates cortical precursor cell proliferation in vitro via muscarinic receptor activation and MAP kinase phosphorylation.
SO European journal of neuroscience, (2000 Apr) 12 (4) 1227-40.
Journal code: 8918110. ISSN: 0953-816X.

L9 ANSWER 41 OF 143 MEDLINE on STN
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SO Molecular pharmacology, (2000 Feb) 57 (2) 278-87.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 42 OF 143 MEDLINE on STN
TI Correlation between low/high affinity ratios for 5-HT(1A) receptors and intrinsic activity.
SO European journal of pharmacology, (1999 Dec 10) 386 (1) 97-103.

Journal code: 1254354. ISSN: 0014-2999.

L9 ANSWER 43 OF 143 MEDLINE on STN
TI The proximal portion of the COOH terminus of the oxytocin receptor is required for coupling to g(q), but not g(i). Independent mechanisms for elevating intracellular calcium concentrations from intracellular stores.
SO Journal of biological chemistry, (1999 Oct 1) 274 (40) 28682-9.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 44 OF 143 MEDLINE on STN
TI Inhibition of GTPase activity of Gi proteins and decreased agonist affinity at M2 muscarinic acetylcholine receptors by spermine and methoctramine.
SO British journal of pharmacology, (1999 Jun) 127 (4) 1021-9.
Journal code: 7502536. ISSN: 0007-1188.

L9 ANSWER 45 OF 143 MEDLINE on STN
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SO Molecular pharmacology, (1999 Aug) 56 (2) 429-33.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 46 OF 143 MEDLINE on STN
TI Melatonin promotes osteoblast differentiation and bone formation.
SO Journal of biological chemistry, (1999 Jul 30) 274 (31) 22041-7.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 47 OF 143 MEDLINE on STN
TI Comparison of the ligand binding and signaling properties of human dopamine D(2) and D(3) receptors in Chinese hamster ovary cells.
SO Journal of pharmacology and experimental therapeutics, (1999 Aug) 290 (2) 908-16.
Journal code: 0376362. ISSN: 0022-3565.

L9 ANSWER 48 OF 143 MEDLINE on STN
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SO Molecular and cellular endocrinology, (1999 Mar 25) 149 (1-2) 1-7.
Journal code: 7500844. ISSN: 0303-7207.

L9 ANSWER 49 OF 143 MEDLINE on STN
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SO Naunyn-Schmiedeberg's archives of pharmacology, (1999 Apr) 359 (4) 295-302.
Journal code: 0326264. ISSN: 0028-1298.

L9 ANSWER 50 OF 143 MEDLINE on STN
TI Activation of protein kinase C modulates alpha2-adrenergic signalling in rat pancreatic islets.
SO Cellular signalling, (1998 Oct) 10 (9) 637-43.
Journal code: 8904683. ISSN: 0898-6568.

L9 ANSWER 51 OF 143 MEDLINE on STN
TI Receptor-independent activation of atrial muscarinic potassium channels in the absence of nucleotides.
SO Journal of biological chemistry, (1998 Oct 30) 273 (44) 28868-72.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 52 OF 143 MEDLINE on STN
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SO Recent progress in hormone research, (1998) 53 25-42. Ref: 77
Journal code: 0404471. ISSN: 0079-9963.

L9 ANSWER 53 OF 143 MEDLINE on STN
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SO European journal of neuroscience, (1998 Jun) 10 (6) 2037-45.
Journal code: 8918110. ISSN: 0953-816X.

L9 ANSWER 54 OF 143 MEDLINE on STN
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SO Journal of neurochemistry, (1998 Sep) 71 (3) 980-90.
Journal code: 2985190R. ISSN: 0022-3042.

L9 ANSWER 55 OF 143 MEDLINE on STN
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SO British journal of pharmacology, (1998 Jun) 124 (3) 485-92.

Journal code: 7502536. ISSN: 0007-1188.

L9 ANSWER 56 OF 143 MEDLINE on STN
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SO Journal of neurochemistry, (1998 Jun) 70 (6) 2273-8.
Journal code: 2985190R. ISSN: 0022-3042.

L9 ANSWER 57 OF 143 MEDLINE on STN
TI Protean agonism at alpha2A-adrenoceptors.
SO Molecular pharmacology, (1998 May) 53 (5) 963-8.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 58 OF 143 MEDLINE on STN
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SO Molecular pharmacology, (1998 May) 53 (5) 808-18.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 59 OF 143 MEDLINE on STN
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SO Journal of biological chemistry, (1998 Apr 24) 273 (17) 10690-5.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 60 OF 143 MEDLINE on STN
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SO Journal of receptor and signal transduction research, (1998 Jan) 18 (1) 25-49.
Journal code: 9509432. ISSN: 1079-9893.

L9 ANSWER 61 OF 143 MEDLINE on STN
TI Switching of the coupling of the beta2-adrenergic receptor to different G proteins by protein kinase A.
SO Nature, (1997 Nov 6) 390 (6655) 88-91.
Journal code: 0410462. ISSN: 0028-0836.

L9 ANSWER 62 OF 143 MEDLINE on STN
TI Canine mast cell adenosine receptors: cloning and expression of the A3 receptor and evidence that degranulation is mediated by the A2B receptor.
SO Molecular pharmacology, (1997 Nov) 52 (5) 846-60.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 63 OF 143 MEDLINE on STN
TI The mu-opioid receptor down-regulates differently from the delta-opioid receptor: requirement of a high affinity receptor/G protein complex formation.
SO Molecular pharmacology, (1997 Jul) 52 (1) 105-13.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 64 OF 143 MEDLINE on STN
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SO Biochemical and biophysical research communications, (1997 Jun 9) 235 (1) 242-8.
Journal code: 0372516. ISSN: 0006-291X.

L9 ANSWER 65 OF 143 MEDLINE on STN
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SO Mechanisms of ageing and development, (1997 Mar) 94 (1-3) 199-211.
Journal code: 0347227. ISSN: 0047-6374.

L9 ANSWER 66 OF 143 MEDLINE on STN
TI RGS4 inhibits Gq-mediated activation of mitogen-activated protein kinase and phosphoinositide synthesis.
SO Journal of biological chemistry, (1997 May 2) 272 (18) 11924-7.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 67 OF 143 MEDLINE on STN
TI Multiple G-protein involvement in parathyroid hormone regulation of acid production by osteoclasts.
SO Journal of cellular biochemistry, (1997 Jan) 64 (1) 161-70.
Journal code: 8205768. ISSN: 0730-2312.

L9 ANSWER 68 OF 143 MEDLINE on STN
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SO Journal of biological chemistry, (1997 Jan 10) 272 (2) 773-81.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 69 OF 143 MEDLINE on STN

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SO Journal of cellular physiology, (1996 Dec) 169 (3) 448-54.
Journal code: 0050222. ISSN: 0021-9541.

L9 ANSWER 70 OF 143 MEDLINE on STN
TI Analysis of lysophophatidylcholine-induced endothelial dysfunction.
SO Journal of cardiovascular pharmacology, (1996 Sep) 28 (3) 345-52.
Journal code: 7902492. ISSN: 0160-2446.

L9 ANSWER 71 OF 143 MEDLINE on STN
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SO Brain research, (1996 Aug 12) 729 (2) 156-69.
Journal code: 0045503. ISSN: 0006-8993.

L9 ANSWER 72 OF 143 MEDLINE on STN
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SO European journal of pharmacology, (1996 Jan 18) 296 (1) 113-8.
Journal code: 1254354. ISSN: 0014-2999.

L9 ANSWER 73 OF 143 MEDLINE on STN
TI Cellular mechanisms underlying adenosine actions on cholinergic transmission in enteric neurons.
SO American journal of physiology, (1996 Jul) 271 (1 Pt 1) C264-75.
Journal code: 0370511. ISSN: 0002-9513.

L9 ANSWER 74 OF 143 MEDLINE on STN
TI Characterization and regulation of the human ML1A melatonin receptor stably expressed in Chinese hamster ovary cells.
SO Molecular pharmacology, (1996 Jul) 50 (1) 166-74.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 75 OF 143 MEDLINE on STN
TI Genetic evidence for involvement of multiple effector systems in alpha 2A-adrenergic receptor inhibition of stimulus-secretion coupling.
SO Molecular pharmacology, (1996 Jul) 50 (1) 96-103.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 76 OF 143 MEDLINE on STN
TI Analysis of inverse agonism at the delta opioid receptor after expression in Rat 1 fibroblasts.
SO Biochemical journal, (1996 Apr 1) 315 (Pt 1) 227-34.
Journal code: 2984726R. ISSN: 0264-6021.

L9 ANSWER 77 OF 143 MEDLINE on STN
TI Activation of phosphatidylinositol 3-kinase by concanavalin A through dual signaling pathways, G-protein-coupled and phosphotyrosine-related, and an essential role of the G-protein-coupled signals for the lectin-induced respiratory burst in human monocytic THP-1 cells.
SO Biochemical journal, (1996 Apr 15) 315 (Pt 2) 505-12.
Journal code: 2984726R. ISSN: 0264-6021.

L9 ANSWER 78 OF 143 MEDLINE on STN
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SO Journal of biochemistry, (1995 Sep) 118 (3) 650-7.
Journal code: 0376600. ISSN: 0021-924X.

L9 ANSWER 79 OF 143 MEDLINE on STN
TI G protein G alpha i-2 inhibits outwardly rectifying chloride channels in human airway epithelial cells.
SO American journal of physiology, (1995 Aug) 269 (2 Pt 1) C451-6.
Journal code: 0370511. ISSN: 0002-9513.

L9 ANSWER 80 OF 143 MEDLINE on STN
TI Expression of the human 5-hydroxytryptamine1A receptor in Sf9 cells. Reconstitution of a coupled phenotype by co-expression of mammalian G protein subunits.
SO Journal of biological chemistry, (1995 Aug 4) 270 (31) 18691-9.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 81 OF 143 MEDLINE on STN
TI Effects of Bordetella pertussis toxin pretreatment on the antiarrhythmic action of ischaemic preconditioning in anaesthetized rats.
SO British journal of pharmacology, (1995 Feb) 114 (4) 755-60.
Journal code: 7502536. ISSN: 0007-1188.

L9 ANSWER 82 OF 143 MEDLINE on STN
TI Alterations in G-proteins in congestive heart failure in cardiomyopathic (UM-X7.1) hamsters.
SO Molecular and cellular biochemistry, (1994 Nov 23) 140 (2) 163-70.

Journal code: 0364456. ISSN: 0300-8177.

L9 ANSWER 83 OF 143 MEDLINE on STN
TI Distinct mechanisms regulate 5-HT2 and thrombin receptor desensitization.
SO Journal of biological chemistry, (1995 Mar 3) 270 (9) 4813-21.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 84 OF 143 MEDLINE on STN
TI Dual pathways for GTP-dependent regulation of chemoattractant-activated K+ conductance in murine J774 monocytes.
SO Journal of biological chemistry, (1994 Dec 16) 269 (50) 31533-43.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 85 OF 143 MEDLINE on STN
TI Pertussis toxin blocks M2 muscarinic receptor-mediated effects on contraction and cyclic AMP in the guinea pig ileum, but not M3-mediated contractions and phosphoinositide hydrolysis.
SO Journal of pharmacology and experimental therapeutics, (1994 Nov) 271 (2) 1042-50.
Journal code: 0376362. ISSN: 0022-3565.

L9 ANSWER 86 OF 143 MEDLINE on STN
TI Regulation of the CHAPS-solubilized muscarinic receptors by an inhibitory GTP binding protein (Gi) in the brain of neonatal and adult rats.
SO Comparative biochemistry and physiology. Physiology, (1994 Oct) 109 (2) 255-67.
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L9 ANSWER 87 OF 143 MEDLINE on STN
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SO Circulation, (1994 Sep) 90 (3) 1225-38.
Journal code: 0147763. ISSN: 0009-7322.

L9 ANSWER 88 OF 143 MEDLINE on STN
TI Alpha 2A-adrenergic receptors activate protein kinase C in human platelets via a pertussis toxin-sensitive G-protein.
SO FEBS letters, (1994 Feb 14) 339 (1-2) 79-83.
Journal code: 0155157. ISSN: 0014-5793.

L9 ANSWER 89 OF 143 MEDLINE on STN
TI Activation of heterologously expressed D3 dopamine receptors: comparison with D2 dopamine receptors.
SO Molecular pharmacology, (1994 Jan) 45 (1) 51-60.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 90 OF 143 MEDLINE on STN
TI A deletion mutation in the third cytoplasmic loop of the mouse m1 muscarinic acetylcholine receptor unmasks cryptic G-protein binding sites.
SO Journal of biological chemistry, (1993 Oct 15) 268 (29) 21734-8.
Journal code: 2985121R. ISSN: 0021-9258.

L9 ANSWER 91 OF 143 MEDLINE on STN
TI Mutation of an aspartate at residue 89 in somatostatin receptor subtype 2 prevents Na+ regulation of agonist binding but does not alter receptor-G protein association.
SO Molecular pharmacology, (1993 Aug) 44 (2) 380-4.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 92 OF 143 MEDLINE on STN
TI Endothelin- and ATP-induced inhibition of adenylyl cyclase activity in C6 glioma cells: role of Gi and calcium.
SO Molecular pharmacology, (1993 Jul) 44 (1) 158-65.
Journal code: 0035623. ISSN: 0026-895X.

L9 ANSWER 93 OF 143 MEDLINE on STN
TI Guanine nucleotide binding proteins mediate D2 dopamine receptor activation of a potassium channel in rat lactotrophs.
SO Journal of physiology, (1993 Mar) 462 563-78.
Journal code: 0266262. ISSN: 0022-3751.

L9 ANSWER 94 OF 143 MEDLINE on STN
TI The mechanism for the rapid desensitization in bradykinin-stimulated inositol monophosphate production in NG108-15 cells involves interaction of a single receptor with multiple signaling pathways.
SO Journal of pharmacology and experimental therapeutics, (1993 Jul) 266 (1) 253-61.
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L9 ANSWER 95 OF 143 MEDLINE on STN
TI Gi alpha 3 and G(o) alpha selectively associate with the cloned somatostatin receptor subtype SSTR2.
SO Journal of biological chemistry, (1993 May 25) 268 (15) 10721-7.

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L9 ANSWER 96 OF 143 MEDLINE on STN
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L9 ANSWER 97 OF 143 MEDLINE on STN
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TI Acetylcholine-mediated K+ channel activity in guinea-pig atrial cells is supported by nucleoside diphosphate kinase.
SO Pflugers Archiv : European journal of physiology, (1993 Jan) 422 (4) 316-24.
Journal code: 0154720. ISSN: 0031-6768.

L9 ANSWER 99 OF 143 MEDLINE on STN
TI Adenosine inhibits fMLP-stimulated adherence and superoxide anion generation by human neutrophils at an early step in signal transduction.
SO Biochimica et biophysica acta, (1993 Feb 17) 1175 (3) 312-8.
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L9 ANSWER 100 OF 143 MEDLINE on STN
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Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 101 OF 143 MEDLINE on STN
TI Regulation of spontaneous opening of muscarinic K+ channels in rabbit atrium.
SO Journal of physiology, (1991 Feb) 433 589-613.
Journal code: 0266262. ISSN: 0022-3751.

L9 ANSWER 102 OF 143 MEDLINE on STN
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L9 ANSWER 103 OF 143 MEDLINE on STN
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L9 ANSWER 104 OF 143 MEDLINE on STN
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L9 ANSWER 105 OF 143 MEDLINE on STN
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L9 ANSWER 107 OF 143 MEDLINE on STN
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L9 ANSWER 109 OF 143 MEDLINE on STN
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L9 ANSWER 110 OF 143 MEDLINE on STN
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L9 ANSWER 111 OF 143 MEDLINE on STN
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L9 ANSWER 113 OF 143 MEDLINE on STN
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L9 ANSWER 117 OF 143 MEDLINE on STN
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L9 ANSWER 120 OF 143 MEDLINE on STN
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L9 ANSWER 121 OF 143 MEDLINE on STN
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L9 ANSWER 127 OF 143 MEDLINE on STN
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L9 ANSWER 129 OF 143 MEDLINE on STN
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Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 130 OF 143 MEDLINE on STN
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L9 ANSWER 131 OF 143 MEDLINE on STN
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Journal code: 8801431. ISSN: 0888-8809.

L9 ANSWER 132 OF 143 MEDLINE on STN
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SO Journal of bone and mineral research : official journal of the American Society for Bone and Mineral Research, (1988 Feb) 3 (1) 81-6.

Journal code: 8610640. ISSN: 0884-0431.

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SO Biochemical pharmacology, (1988 Dec 1) 37 (23) 4549-55.
Journal code: 0101032. ISSN: 0006-2952.

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Journal code: 9316922. ISSN: 0340-6075.

L9 ANSWER 137 OF 143 MEDLINE on STN
TI Serotonin stimulates DNA synthesis in fibroblasts acting through 5-HT1B receptors coupled to a Gi-protein.
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SO Journal of biological chemistry, (1988 May 15) 263 (14) 6491-4.
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SO Journal of cell biology, (1987 Dec) 105 (6 Pt 2) 2959-71.
Journal code: 0375356. ISSN: 0021-9525.

L9 ANSWER 143 OF 143 MEDLINE on STN
TI Development of muscarinic cholinergic inhibition of adenylate cyclase in embryonic chick heart. Its relationship to changes in the inhibitory guanine nucleotide regulatory protein.
SO Journal of biological chemistry, (1986 Jul 5) 261 (19) 9011-21.
Journal code: 2985121R. ISSN: 0021-9258.

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L3: Entry 92 of 99 File: USPT Mar 4, 2003

US-PAT-NO: 6528271
DOCUMENT-IDENTIFIER: US 6528271 B1

TITLE: Inhibition of .beta.arrestin mediated effects prolongs and potentiates opioid receptor-mediated analgesia

DATE-ISSUED: March 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Lin; Fang-Tsyr	Durham	NC		
Caron; Marc G.	Hillsborough	NC		
Lefkowitz; Robert J.	Durham	NC		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Duke University	Durham	NC			02

APPL-NO: 09/469554 [PALM]
DATE FILED: December 22, 1999

PARENT-CASE:
This application is a continuation-in-part of U.S. application Ser. No. 09/233,530, now issued as U.S. Pat. No. 6,110,693, filed Jan. 20, 1999; which is a continuation of U.S. application Ser. No. 08/869,568, now issued as U.S. Pat. No. 5,891,646, filed Jun. 5, 1997.

INT-CL-ISSUED: [07] C07 K 14/00, C07 K 17/00, C12 Q 1/00, G01 N 33/53, G01 N 33/567

US-CL-ISSUED: 435/7.2; 435/4, 530/350
US-CL-CURRENT: 435/7.2; 435/4, 530/350

FIELD-OF-CLASSIFICATION-SEARCH: 424/9.1, 424/9.2, 435/4, 435/7.2, 530/350
See application file for complete search history.

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL

☐	5591618	January 1997	Chantry et al.	435/194
☐	5597699	January 1997	Lanzara	435/7.21
☐	5658783	August 1997	Grandy et al.	435/325
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☐	6007986	December 1999	Sadee	435/6
☐	RE36547	February 2000	Crain et al.	514/282
☐	6028175	February 2000	Grandy et al.	530/350
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☐	6110693	August 2000	Barak et al.	435/7.2

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FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	CLASS
WO98/55635	December 1998	WO	

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ART-UNIT: 1632

PRIMARY-EXAMINER: Baker; Anne-Marie

ATTY-AGENT-FIRM: Burns, Doane, Swecker & Mathis, L.L.P.

ABSTRACT:

The present invention provides a .beta.arrestin knockout mouse useful for screeening compounds for efficacy in controlling pain, methods of controlling pain in subjects by inhibiting binding of .beta.arrestin to phosphorylated .mu. opioid receptors, and methods of screening a compound for activity in potentiating .mu. opioid receptor agonist activity (e.g., morphine activity) by determining whether or not said compound inhibits .beta.arrestin binding to a phosphorylated .mu. opioid receptor.

12 Claims, 8 Drawing figures

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L6: Entry 1 of 3 File: PGPB Apr 14, 2005

DOCUMENT-IDENTIFIER: US 20050079178 A1
TITLE: Inhibitor of cardiac tachyarrhythmias

Detail Description Paragraph:
[0105] Desensitization of G-protein receptors, including .beta.-adrenergic, adenosine, muscarinic, and angiotensin receptors, occurs by: 1) ligand-independent phosphorylation through protein kinase A and 2) ligand-dependent phosphorylation through .beta.-adrenergic receptor kinase. It is proposed that increased .beta.-adrenergic receptor sensitivity and increased isoproterenol-stimulated c-AMP formation results directly from decreased .beta.-adrenergic receptor kinase-1 expression/activity (.beta.-ARK-1) within injured epicardium. .beta.-ARK-1, by phosphorylating ligand-activated .beta.-adrenergic receptors, desensitizes the .beta.-adrenergic receptor and precipitates its internalization from the cell membrane to the cell interior by an obligate transport protein, .beta.-arrestin (Pitcher et al., 1998; Bunemann et al., 1999; Krupnick et al., 1998). .beta.ARK-1, a G-receptor kinase of the superfamily of G-receptor inactivating enzymes, is the principal mechanism providing for the desensitization and the termination of .beta.-adrenergic receptor stimulation in myocardium and other tissues (Pitcher et al., 1998; Bunemann et al., 1999; Krupnick et al., 1998). The decrease of .beta.-ARK-1 in injured myocardium has been determined by direct measurement of myocardial .beta.-ARK-1 activity (FIG. 12), immunoblot of .beta.-ARK-1 expression (FIG. 13A), and immunohistofluorescence of myocardial .beta.-ARK-1 content. Only a partial recovery of .beta.-ARK-1 activity was observed at 96 hours (FIG. 13B). It appears that the decrease in .beta.-ARK-1 in ischemically-injured myocardium results from an increased degradation of .beta.-ARK-1 in ischemically-injured epicardium.

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L3: Entry 34 of 99 File: PGPB May 27, 2004

DOCUMENT-IDENTIFIER: US 20040101887 A1
TITLE: Methods of assaying receptor activity and constructs useful in such methods

Summary of Invention Paragraph:
[0004] It has been postulated that members of the GPCR superfamily desensitize via a common mechanism involving G protein-coupled receptor kinase (GRK) phosphorylation followed by arrestin binding. Gurevich et al., J. Biol. Chem. 270:720 (1995); Ferguson et al., Can. J. Physiol. Pharmacol. 74:1095 (1996). However, the localization and the source of the pool of arrestin molecules targeted to receptors in response to agonist activation was unknown. Moreover, except for a limited number of receptors, a common role for .beta.-arrestin in GPCR desensitization had not been established. The role of .beta.-arrestins in GPCR signal transduction was postulated primarily due to the biochemical observations.

Detail Description Paragraph:
[0036] Phosphorylation of GPCRs is a mechanism leading to desensitization of the receptors; receptors that have been continuously or repeatedly stimulated lose responsiveness, whereas the responses of other receptors remain intact. See Harden, Pharmacol. Rev. 35:5 (1983); Benovic et al., Annu. Rev. Cell. Biol. 4:405(1988). In a variety of cells, specific kinases have evolved for specific GPCRs. Desensitization occurs via the following pathway: agonist occupancy of the receptor transforms the receptor into all appropriate substrate for an associated kinase; .beta.-arrestin binds to the kinase phosphorylated receptor and prevents subsequent interaction with the appropriate G-protein, as well as initiating both internalization and resensitization processes. Ferguson et al, Science, 271:363 (1996); Lohse et al., Science 248:1547 (1990). .beta.-arrestin dependent desensitization is induced only when the GPCR is activated by ligand binding, and is an example of homologous desensitization (i.e., the ligand desensitizes only its target receptors). Lohse et al. (1990) and Attramadal et al., J. Biol. Chem. 267:17882 (1992) provide cDNA and amino acid sequences of .beta.-arrestiin. Various isoforms of .beta.-arrestin are known; as used herein, .beta.-arrestin refers to all such isoforms of .beta.-arrestin, proteins having substantial sequence similarity thereto which are functional .beta.-arrestins, and functional fragments thereof. Functional fragments of .beta.-arrestin, its isoforms and analogs, may be determined using techniques as known in the art.

Detail Description Paragraph:
[0066] The present methods may further be used to assess or study the effects of any molecule in the GPCR pathway which exerts its effect upstream of .beta.-arrestin binding (i.e., prior to .beta.-arrestin binding to the phosphorylated GPCR). Thus the present invention provides methods for assessing GPCR pathway functions in general. As used herein, the GPCR pathway refers to the series of events which starts with agonist activation of a GPCR followed by desensitization of the receptor via G protein-coupled receptor kinase (GRK) phosphorylation and .beta.-arrestin binding.

L3: Entry 52 of 99 File: PGPB Aug 21, 2003

DOCUMENT-IDENTIFIER: US 20030157553 A1
TITLE: Methods of assaying for G protein-coupled receptor ligands and modulators

Summary of Invention Paragraph:
[0004] Signaling by diverse GPCR agonists is believed to be terminated by a uniform two-step mechanism (Freedman and Lefkowitz (1996) Recent Prog. Horm. Res. 51:319-353). According to the model, activated receptor is first phosphorylated by a G protein-coupled receptor kinase (GRK). An arrestin protein then binds to the activated phosphoreceptor, thereby blocking G protein interaction. Arrestin-receptor complex is subsequently internalized, whereupon receptor is either dephosphorylated and recycled back to the plasma membrane (resensitization) or sorted to lysosomes and destroyed (down-regulation). Thus, the formation of the arrestin-receptor complex appears to be the final step of desensitization and the first step of resensitization and/or receptor down-regulation.

Summary of Invention Paragraph:
[0005] GPCRs are activated by an extremely wide variety of external stimuli and are now believed to play a role in regulating the activity of virtually all eukaryotic cells. In contrast, the repertoire of receptor kinases and arrestins involved in the desensitization of these receptors is rather limited: six GRKs and four arrestins have thus far been found in mammals (reviewed in Freedman and Lefkowitz, supra).

Summary of Invention Paragraph:
[0006] The fact that a limited number of receptor kinases and arrestins can regulate desensitization of numerous GPCRs makes these molecules attractive targets for research designed to identify potential modulators of GPCR signaling, in particular modulators of such receptors for use as human therapeutics. The present invention is based, at least in part, on a new use for phosphorylation-independent mutants of arrestin proteins as assay components in screening assays designed to identify ligands and/or modulators of G protein-coupled receptors (GPCRs). In particular, it has been discovered that phosphorylation-independent mutants of arrestin capable of binding GPCRs in a manner independent of the natural requirement for phosphorylation by intracellular receptor kinases. Such phosphorylation-independent mutants of arrestin retain there dependence on agonist for GPCR-binding, however. As such, phosphorylation-independen- t arrestin mutants are particularly well-suited for in vitro assays, for example, in assays that are directed to the identification of natural and surrogate agonists of orphan GPCRs (e.g., of known and/or orphan GPCRs, for example, in orphan GPCR ligand fishing assays). The phosphorylation-independent mutants of arrestin are also particularly well-suited for in vitro assays that are directed to the identification of GPCR antagonists and/or agonists.

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TITLE: Methods of assaying for G protein-coupled receptor ligands and modulators

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INVENTOR-INFORMATION:

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REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The present invention features methods of assaying for ligands and/or modulators of G protein-coupled receptors, for example, orphan G protein-coupled receptors. The methods of the invention feature constitutively active arrestin mutants, in particular, phosphorylation independent mutants. Also described are specific phosphorylation independent arrestin mutants and methods of making such mutants.

RELATED APPLICATIONS

[0001] This application claims the benefit of prior-filed provisional patent application U.S. Ser. No. 60/186,706, entitled "Methods of Assaying for G Protein-Coupled Receptor Ligands and Modulators", filed Mar. 3, 2000 (pending). The content of the above referenced application is incorporated herein in its entirety by this reference.

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L7: Entry 1 of 1 File: PGPB May 23, 2002

DOCUMENT-IDENTIFIER: US 20020062490 A1
TITLE: Hypertension

Summary of Invention Paragraph:
[0004] A functional abnormality leading to hypertension can reflect an imbalance between G protein-coupled receptor (GPCR) mediated vasoconstriction and vasodilation. GPCR signaling is mediated via heterotrimeric G proteins which, following receptor activation, dissociate and release activated G.alpha. and G.beta..gamma. subunits, both of which are capable of molecular signaling (Post et al, FASEB J. 10:741-749 (1996)). One G protein family member, Gq, is activated by several GPCRs mediating vasoconstriction and its activation can dramatically increase systemic vascular resistance (SVR), mean arterial pressure (MAP) and myocardial and vascular hypertrophy. Activation of another member of the G protein family, Gs, by GPCRs including .beta.-adrenergic receptors (ARs), can mediate vasodilation and a decrease in SVR and MAP. Impairment in .beta.AR-mediated vasodilation due to an alteration in receptor/G-protein coupling increases SVR and has been described to occur in both human and animal models of hypertension (Feldman, J. Clin. Invest. 85:647-652 (1990); Feldman et al, Hypertension 26:725-732 (1995)). This defective .beta.AR coupling is accompanied by selective increases in expression and activity of the G protein-coupled receptor kinase 2 (GRK2 or .beta.ARK1) which has been found in the lymphocytes of hypertensive patients (Gros et al, J. Clin. Invest. 99:2087-2093 (1997)). GRK2 phosphorylates and desensitizes agonist-occupied GPCRs, including BARs, and therefore prevents activation of G proteins. Of the 6 members of the GRK family, GRK2, GRK3, GRK5 and GRK6 have been found in VSM (Gros et al, J. Clin. Invest. 99:2087-2093 (1997); Ishizaka et al, J. Biol. Chem. 272:32482-32488 (1997)). Although none of these kinases show substrate selectivity in vitro, recent evidence suggests that in vivo in the heart they show specific actions (Eckhart et al, Circ. Res. 86:43-50 (2000); Koch et al, Ann. Rev. Physiol. 62:237-260)). With respect to important vascular GPCRs, GRK2 desensitizes the .beta..sub.2AR and angiotensin II receptor in vivo, whereas it is ineffective on the .alpha..sub.1BAR (Eckhart et al, Circ. Res. 86:43-50 (2000); Koch et al, Ann. Rev. Physiol. 62:237-260)).

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L3: Entry 18 of 99 File: PGPB Feb 10, 2005

DOCUMENT-IDENTIFIER: US 20050032158 A1
TITLE: Binding assays that use human T1R2 to identify potential taste modulators

Detail Description Paragraph:
[0077] "Inhibitors," "activators," and "modulators" of T1R genes or proteins are used interchangeably to refer to inhibitory, activating, or modulating molecules identified using in vitro and in vivo assays for taste transduction, e.g., ligands, agonists, antagonists, and their homologs and mimetics. Inhibitors are compounds that, e.g., bind to, partially or totally block stimulation, decrease, prevent, delay activation, inactivate, desensitize, or down regulate taste transduction, e.g., antagonists. Activators are compounds that, e.g., bind to, stimulate, increase, open, activate, facilitate, enhance activation, sensitize, or up regulate taste transduction, e.g., agonists. Modulators include compounds that, e.g., alter the interaction of a receptor with: extracellular proteins that bind activators or inhibitor (e.g., ebnerin and other members of the hydrophobic carrier family); G proteins; kinases (e.g., homologs of rhodopsin kinase and beta adrenergic receptor kinases that are involved in deactivation and desensitization of a receptor); and arrestins, which also deactivate and desensitize receptors. Modulators can include genetically modified versions of T1R family members, e.g., with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, small chemical molecules and the like. Such assays for inhibitors and activators include, e.g., expressing T1R family members in cells or cell membranes, applying putative modulator compounds, in the presence or absence of taste stimuli, e.g., sweet taste stimuli, and then determining the functional effects on taste transduction, as described above. Samples or assays comprising T1R family members that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of modulation. Control samples (untreated with modulators) are assigned a relative T1R activity value of 100%. Inhibition of a T1R is achieved when the T1R activity value relative to the control is about 80%, optionally 50% or 25-0%. Activation of a T1R is achieved when the T1R activity value relative to the control is 110%, optionally 150%, optionally 200-500%, or 1000-3000% higher.

Detail Description Paragraph:
[0201] Activated GPCR receptors become substrates for kinases that phosphorylate the C-terminal tail of the receptor (and possibly other sites as well). Thus, activators will promote the transfer of 32P from gamma-labeled GTP to the receptor, which can be assayed with a scintillation counter. The phosphorylation of the C-terminal tail will promote the binding of arrestin-like proteins and will interfere with the binding of G proteins. The kinase/arrestin pathway plays a key role in the desensitization of many GPCR receptors. For example, compounds that modulate the duration a taste receptor stays active would be useful as a means of prolonging a desired taste or cutting off an unpleasant one. For a general review of GPCR signal transduction and methods of assaying signal transduction, see, e.g., Methods in Enzymology, vols. 237 and 238 (1994) and volume 96 (1983); Bourne et al., Nature, 10:349:117-27 (1991); Bourne et al., Nature, 348:125-32 (1990); Pitcher et al., Annu. Rev. Biochem., 67:653-92 (1998).